October 29, 2003

Edwin L. Mongan
Manager, Environmental Stewardship
E.I. du Pont de Nemours & Company, Inc.
1007 Market Street
DuPont 6082
Wilmington, DE 19898

Dear Mr. Mongan:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Carbamate Hydrochloride posted on the ChemRTK HPV Challenge Program Web site on June 26, 2003. I commend E.I. du Pont de Nemours for their commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed Comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that DuPont advise the Agency, within 60 days of this posting on the Web site, of any modifications to their submission. Please send any electronic revisions or comments to the following addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
Carbamate Hydrochloride

Summary of EPA Comments

The sponsor, E. I. du Pont de Nemours & Company, submitted on May 23, 2003, a test plan and robust summaries to EPA for Carbamate Hydrochloride (CAS No. 65206-90-8) dated December 17, 2002. EPA posted the submission on the ChemRTK HPV Challenge Web site on June 26, 2003.

EPA has reviewed this submission and reached the following conclusions:

1. Substance Characterization. Clarifying information on the manufactured substance is needed.

2. Physicochemical Properties. The submitter needs to recalculate the log K_{ow} value.

3. Environmental Fate. The submitter needs to provide estimated photodegradation data; provide measured biodegradation and stability in water data; and recalculate fugacity model.

4. Health Effects. (a) EPA agrees with the submitter's plan to conduct genetic and developmental toxicity studies. (b) The submitter needs to provide additional information to satisfy the requirements for classification of carbamate hydrochloride as a "closed system intermediate." (c) As an alternative to the developmental toxicity test proposed, per HPV Challenge Program guidance EPA recommends a combined repeated-dose/reproductive/developmental toxicity screening test.

5. Ecological Effects. EPA agrees with the submitter that acute testing is needed for all ecological endpoints.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on the Carbamate Hydrochloride Challenge Submission

Substance Characterization

The test plan describes carbamate hydrochloride as a solid that is shipped in solution. The submitter needs to clarify whether a solid product occurs in the manufacturing process.

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

Adequate data are available for melting point, boiling point, vapor pressure, and water solubility for the purposes of the HVP Challenge Program, if a preformulation non-aqueous product is not isolated. Otherwise, measured data need to be generated according to OECD guidelines.

Partition coefficient. The submitter reports an estimated log K_{ow} of -0.07 using KOWWIN v. 166. EPA obtained an identical value using a SMILES notation of CCOC(=O)N(C)C=NN(C)C. However, this notation does not represent the structure of carbamate hydrochloride. The correct notation is O=C(OCC)N(C)C(=N(H)(H)(Cl))N(C)C, which produces a value of -3.96. The submitter needs to use the correct SMILES notation and recalculate the partition coefficient.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

Photodegradation. The submitter needs to provide data for this endpoint; estimated data using EPIWIN are acceptable.

Stability in water. The test plan reports that this chemical hydrolyzes very slowly (>10 years at pH 7; estimate from HYDROWIN v. 1.67). The submitter needs to provide measured data.

Biodegradation. In table 1 of the robust summary, the submitter indicates that carbamate hydrochloride is readily biodegradable as estimated using BIOWIN. This conclusion cannot be inferred from estimated data. The submitter needs to provide measured biodegradation data following OECD TG 301.

Fugacity. The submitter's use of the level III model is adequate. However, the submitter needs to recalculate its fugacity model using appropriately corrected or measured physicochemical values.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

Adequate data are available for acute toxicity. EPA agrees with the submitter's plan to conduct developmental toxicity testing and genetic toxicity studies. The submitter requests an exemption from repeated-dose and reproductive toxicity testing based on EPA's guidelines for closed-system intermediates.

Repeated-dose and reproductive toxicity. No data were submitted for these endpoints and no testing is proposed, because of the submitter's assertion that carbamate hydrochloride is a closed-system intermediate.

The Guidance for Testing Closed System Intermediates for the Challenge Program http://www.epa.gov/chemrtk/guidocs.htm allows for a reduced testing protocol provided certain criteria are met. The information required to judge a "closed-system intermediate" claim must address the following:

I. Site information
    A. Number of sites.
    B. Basis for "closed process" conclusion at each site.
        1) Process description.
        2) Monitoring data showing no detection.
        3) In the absence of monitoring data, the basis for believing that releases do not occur.
    C. Data on "presence in distributed products."
II. Information on transport (mode, volume, controls, etc)
III. A data search showing that the chemical is not present in other end products.

EPA does not believe that the information provided by the submitter is adequate to satisfy the requirements for classification as a "closed system intermediate" eligible for reduced testing in the HPV Challenge Program.

The test plan states that carbamate hydrochloride is manufactured at a U.S. facility and transported to another location of the same company, where the chemical is consumed in a multistep process. Although the submitter states that it produces and further reacts carbamate hydrochloride in completely closed systems, neither process descriptions nor flow diagrams are provided. A more complete description of the manufacturing and processing processes is needed. Further, the submitter provides no monitoring data for manufacturing, loading and unloading of railcars and trucks, or consumption of the chemical during the series of chemical reactions. Monitoring data or other justification are needed to document that exposure does not occur from the open railcar dome during loading and unloading of the chemical or during manufacture and consumption of the chemical.

EPA therefore reserves judgment on whether carbamate hydrochloride meets the criteria for a "closed system intermediate," pending the submission of additional information. Alternatively, the submitter may conduct a combined repeated-dose/reproductive/developmental toxicity screening test (OECD TG 422)

instead of the proposed developmental toxicity study (OECD TG 414), which would then satisfy the repeated-dose and reproductive toxicity endpoints and obviate the need to sustain a “closed system intermediate” claim.

Developmental toxicity. The submitter plans to conduct a developmental toxicity test (OECD TG 414). However, HPV Challenge Program guidance recommends that a combined screening test (OECD TG 421 or 422) be used.

Ecological Effects (fish, invertebrates, and algae)

Fish, invertebrates, and algae. EPA agrees with the submitter’s plan to conduct acute toxicity tests to satisfy these endpoints.

Specific Comments on the Robust Summaries

Environmental Fate

Fugacity. The submitter needs to include the input values used for the fugacity estimation

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.